

## Surgical Oncology (Session 1)

### The rectal cancer in the elderly patients

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**INTRODUCTION:** The aim of study is looking at surgically complicated and anatomopathologically advanced kinds of colonic-rectal cancer in over eighty years old patients

**METHODS:** The study is leaded on 299 patients operated in the First Surgical Dept. of University of Bari from 1978 to 1998. We affected 27 pt. over the eighty (9 %; average age 83.5 aa.; 15 male and 12 female), 16 operated on emergency, 11 on choice. The tumor was placed in the rectum in 9 pt., in 12 pt. in the sigmoid colon and sigmoid-rectal connection and left colon, in 2 pt. in the transverse colon, in 4 in the right colon. Moreover we affected these patients under a modified Dukes classification : 0 pt. (0 %), A, 5 pt. (20 %) B1, 3 pt. (12 %) B2, 1 pt. (3 %) C1, 5 pt. (17 %) C2, 1 pt. (3 %) D, 12 pt. (40 %) valued during operation with no-resectable advanced disease. The patients underwent at this kind of operations : 11 stoma sec. Mixer, 3 Miles, 7 Hartmann, 5 resection and anastomosis, 1 ileo- transverse anastomosis. **RESULTS :** The rate of over eighty patients operated in emergency was 59 % (16 pt.), for those under age it was 12 % (33 pt.), (19/27 vs 104/272,  $p<0.0001$ ).

In the over eighty patients the tumors interesting the rectum and the left colon was 80 %, in those under age was 72 %. The istological and intraoperative examen, showed that a greater frequency of advanced tumors in over eighty patients was 70 % (19 pt. whit C1- C2- D – advanced tumors), than 38 % (95 pt.). Surgically it was possible to made resection and anastomosis in 5 pt. (18.5 %).

**OUTCOMES:** A greater frequency of advanced tumors in over eighty pt. seems to be justified from a lower biological aggressiveness with a long time during the tumor is silent, but surely from careless on the typical colonic-rectal tumor symptoms too. It justifies the higher frequency of surgical emergency (59 %) and the lower rate of oncologically effective resection and anastomosis (18.5 %). It's very important for the surgeon to pay attention to the slight symptoms of colonic-rectal cancer in the patients, who, whit the increasing of mean age, always most frequently they will be geriatrics.

### GASTRIC LYMPHOMA: OUR EXPERIENCE

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#### INTRODUCTION

The primitive gastric lymphoma represents, today, the 2-4,5% of all gastric neoplasms. The pre-operative diagnosis most of the time is not always possible. Therefore surgery has a primary importance in staging and in therapy, in the initial stage of the neoplasm.

#### MATERIALS AND METHODS

From January 1990 to December 1997 we treated 15 patients affected from primitive gastric lymphoma: 8 women and 7 men, medium age 56 years. The preoperative staging at the time of the diagnosis: 7 patients were in stage I E, 5 patients in stage II E 1, 3 patients in stage III E. The surgical intervention was total gastrectomy (9 patients) and partial gastrectomy 4/5 (6 patients) together with lymphadenectomy and omentectomy. The complementary chemotherapy was given to 7 patients.

#### RESULTS

Of 15 patients that received the surgical treatment two had postoperative complications: pneumonia and TIA. The operative mortality was zero. All patients were put in follow-up and it was continued until December 1998. Of the 15 patients two died as a consequence of the illness and one died from other causes.

#### DISCUSSION

The primitive gastric lymphoma represents the 2-4,5% of all gastric neoplasm and its location, in the 55-65% of causes, is on level of the gastric body. There are concrete possible treatment and cures especially in the initial stage I E of the neoplasm (dimension inferior to 7cm). For the intermediate stage surgery accompanied with chemotherapy, reduces the neoplasm mass, while in the stages III and IV has used only for palliative reasons.

#### CONCLUSION

The non-Hodgkin gastric lymphoma has a prognosis less serious than gastric neoplasm, with a global survival about 50%. Surgery is the better therapy for treatment in stage I E and in the intermediate stage, but it has acquired an important role also in advanced stages accompanied with adequate complementary therapy.

### PERITONEAL CARCINOMATOSIS: THE INTEGRATE TREATMENT

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**INTRODUCTION:** The transperietal diffusion of an endoabdominal malignancy may develop into a massive peritoneal carcinomatosis without hematogenic metastatization. It is true for some low-grade malignant tumors, that lack of infiltrative attitude and "redistribute" on the peritoneum as an effect of gravity, intestinal peristaltic movements and peritoneal reabsorption. The traditional surgery target has often been palliation, while the surgical intent should be to obtain a complete tumor cytoreduction removing the peritoneum together with the neoplastic implants. After cytoreduction immediate intra- or postoperative abdominal antitublastic infusion provides a direct contact between the drug and the residual free neoplastic cells when they are entirely exposed and before fibrin placement, inflammation mediators and growth factors production.

**METHODS:** Total peritonectomy can be summarized as the complete removal of all the parietal peritoneum and the visceral peritoneum involved by disease together with glissonectomy, cholecystectomy, splenectomy, minus and majus omentectomy, sigmoidectomy and hysterannexectomy; the operation is completed removing every visceral disease, including gastric antrum if necessary. Before performing the intestinal anastomoses, hyperthermic antitublastic perfusion is carried out throughout the abdomen for 90 minutes at a temperature of 41.5-42.5° C: MMC (3.3 mg/m<sup>2</sup>/L of perfusate) and CDDP (25 mg/m<sup>2</sup>/L of perfusate) are introduced into the perfusion circuit in the event of a carcinosis from appendicular or colorectal primary, while CDDP alone is utilized for ovarian tumors.

**RESULTS:** Between April 1995 and December 1998, 35 patients, with a mean age of 50 years (range, 17 to 70) affected by extensive peritoneal carcinomatosis, mainly from ovarian and colorectal primary, were submitted to peritonectomy. Peritonectomy was total in more than half of the cases because of the widely diffused carcinomatosis and lead to a complete cyto reduction (CC-0) in all the patients but 3. Complications rate was 50%, while mortality rate was 12% with no new events after a learning curve of 18 mos. Presently, after a median follow-up of 17 mos, the two-yr overall survival is 55.2%, with a median survival of 26mos.

**CONCLUSIONS:** The curative potential of this combined therapeutic approach seems high in stage IV patients with peritoneal carcinomatosis from ovarian or colorectal primary not responding to systemic chemotherapy. The surgical learning curve is clearly leading towards shorter operation time and lower intraoperative blood loss with a poportional mortality decrease. The selection criteria of patients can strictly affect the surgical risk and the postoperative outcome and such combined treatment has to be reserved for controlled clinical trials.

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# MICROSATELLITE INSTABILITY AND SPORADIC COLORECTAL CANCER

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**Background** Alteration of the length of simple repetitive genomic sequences, microsatellite instability (MSI) characterises a distinct mechanism of colorectal carcinogenesis. MSI is intrinsic to most colorectal carcinoma (CRC) from patients with hereditary non polyposis colorectal cancer (HNPCC), reflecting germline mutations in the mismatch-repair (MMR) genes. MSI has also been reported in a subset of sporadic colorectal carcinomas (SCRC) (13-17%) but its occurrence and chronological sequence in the development of SCRC appears less well defined.

To explore the time sequence in acquisition of MSI, and the role it plays during tumor progression in SCRC, we studied the incidence of MSI in tissue samples from patients with SCRC at 7 different microsatellite loci.

**Purpose** Aim of this study is to analyse a consecutive series of SCRC with the purpose to establish the incidence of MSI and the clinical and pathological features of the MSI positive cases.

**Method** From January 1997 our group in collaboration with the Institute of Genetic, has begun a prospective study on the SCRC and MSI. We observed sixty patients with initial diagnosis of SCRC; 9 stage I, 31 stage II, 12 stage III and 8 stage IV were included in this study. At this moment we have just examined 38 cases for the presence of MSI (3 stage I, 23 stage II, 7 stage III and 5 stage IV). After the extraction of the DNA with polymerase chain reaction (PCR) method, we analysed in all cases BAT25 and BAT26, loci currently considered more sensitive for MSI.

**Results** Of the 38 cases currently analysed in the search of MSI, 3 positive cases were found for MSI. Two out of three were stage II tumors located in the right colon. Pathological type was adenocarcinoma and one alone had extracellular mucin production. The third patient had a tumor located in the left colon, the stage was IV (T4N0M1) and the pathological type was adenocarcinoma with grading G3. The patients were aged respectively 81, 76 and 63 years.

**Discussion and Conclusion** Even if the data are preliminary MSI has been found in a subset of SCRC (8%). This could have a different meaning in comparison to HNPCC. In these cases tumor progression may involve increased genetic instability and MSI could design a late stage of tumor progression or a different degree of tumor aggressiveness. To clarify the role of MSI will be useful to have an higher number of patients to correlate MSI with prognosis and drug response.

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2) Senba S, Konishi F, Okamoto T, Kashiwagi H, Kanazawa K, Miyaki M, Konishi M, Tsukamoto T *Clinicopathologic and genetic features of nonfamilial colorectal carcinomas with DNA replication errors* *Cancer* 1998 Jan 15; 82(2):279-285

# COLONIC J-POUCH-ANAL ANASTOMOSIS FOR CIRCUMFERENTIAL RECTAL VILLOUS ADENOMA.

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**Introduction:** Straight coloanal anastomosis is a well-established technique in the surgical therapy of tumours of the inferior third of the rectum, but pts with preoperative low anal tone often experience urgency and fecal soiling. The use of a pelvic pouch seems to improve functional results. Complete rectal prolapse may require resective surgery, rarely total rectal excision.

**Case report:** A 73-year-old pluriparous woman experienced mucous diarrhoea for 2 years. Then the onset of rectal prolapse causing fecal incontinence, which eventually became non reducible, the pt was therefore admitted to our unit. On inspection, a complete rectal prolapse with mucosal polypoids aspects was observed and carefully reduced. Colonoscopy showed multiple diverticulosis of the left colon and polypoids aspects of the last 7 cm of the whole circumference of the rectum. Histology confirmed the

presence of villous adenoma. Ano-rectal manometry showed low values of anal resting pressure (ARP), maximum resting pressure (MRP), and maximum voluntary contraction (MVC). The recto-anal inhibitory reflex (RAIR) was present at 40 ml air, maximum tolerated volume (MTV) (220 ml air) was normal. The pt underwent colonic "J" pouch-anal anastomosis. The mobilized splenic flexure and the descending colon were made into a 7 cm reservoir using linear staplers. The pouch was anastomosed to the anum at the dentate line using interrupted sutures. A defunctioning stoma was not employed. The surgical specimen showed mucosal polypoids appearance extending circumferentially 7 cm above the dentate line (villous adenoma, low-grade dysplasia). The postop. course was uneventful. Three and 9 months postop stool frequency/24 h was 2x/day and the pt was fully continent. Ano-rectal manometry showed the following values: ARP: 20 and 32 mmHg at 3 and 2 cm from the anal verge; MRP 44 mmHg; MVC 40 mmHg; MTV 180 ml air; the RAIR was negative at 60 ml air. Proctography showed good distensibility of the colonic reservoir, with complete emptying of the neorectum and anorectal angles within the normal range. **Conclusions:** The choice to perform coloanal anastomosis with colonic reservoir was rewarded by the good functional results obtained after the first month of adaptation. The increase in anal resting tone and voluntary contraction, together with the good capacity of the neorectum seems to be the cause of such improvement, whereas the loss of RAIR does not seem to affect continence in this case.

# PREOPERATIVE RADIOTHERAPY AND ENDOLUMINAL TRANSANAL RESECTION AND ANASTOMOSIS USING FIBRIN GLUE OF LOW RECTAL NEOPLASMS

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**INTRODUCTION.** Many experimental and clinical studies demonstrated that fibrin glue promotes the healing of colonic anastomoses. The fibrin glue results highly effective in resective endoluminal colonic surgery, in which the technical difficulties in performing the colonic anastomosis lead to anastomotic dehiscence and fistulas. **METHODS.** In the last 4 years, we performed resective endoluminal colonic surgery in 5 patients, 49-72 years old, with a preoperative diagnosis of cancer of the rectum (T2-T3NxMx). All patients, studied by MR scan and immunoscintigraphy, refused the Miles operation; on the other hand, in all patient the low localisation of the tumour prevented from performing coloanal anastomosis. We decided to submit the patient to conservative procedure, consisting in preoperative radiotherapy (40 Gy daily for four weeks with a linear accelerator) and local endoluminal excision of the mass. The operation consisted in the transanal resection of the tumor using a Nd-YAG laser delivered on a 800 micron contact fibre under a 10 mm scope guide; the anastomotic lips were approximated by 4-5 2/0 absorbable interrupted stitches, and the anastomosis was coated with 2 cc of fibrin glue. All patients received a postoperative total parenteral nutrition for 7 days; the postoperative course was uneventful. Four weeks after surgery, all patients underwent adjuvant therapy (5-FU). **RESULTS.** All patient survived the operation; the postoperative course was uneventful. The follow-up, lasted 9-48 months, didn't reveal neither local nor systemic recurrences. **DISCUSSION AND CONCLUSIONS.** The main technical difficulty in performing endoluminal as well as endoscopic colonic surgery is to carry out the anastomosis. In our precedent works, we demonstrated the feasibility of colonic laparoscopic anastomosis using 4-5 interrupted stitches and fibrin glue (1). This technique is effective in patients with rectal malignancies that reject the Miles operation when the coloanal anastomosis is not feasible. The association of combined radio-chemotherapy allows to obtain a prolonged follow-up without local or systemic recurrences.

# RATIONAL MANAGEMENT OF MALIGNANT COLON POLYPS AND ENDOSCOPIC FOLLOW-UP

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Reduction in colorectal cancer (CRC) mortality can be achieved through detection and treatment of early stage CRC and identification and removal of adenomatous polyps, putting into practice an effective plan of secondary prevention. **Background.** The aims of this study were to evaluate our treatment strategy for invasive adenocarcinoma in colorectal malignant polyps and thereby the long term outcome and survival of patients, and to define guidelines for endoscopic surveillance post-polypectomy. **Materials and methods.** Over a 16-years period (1992-1998) we removed 1799 polyps from 1160 patients, 733 males (63.1%), 427 females (36.8%), mean age 59.85 (range 7-91). 1336 polyps were sessile, 463 pedunculated. Endoscopic control at 1 year intervals was recommended in all patients after surgical or endoscopic resection. **Results.** In 45 pts (2.5%) the polypectomy specimen (16 pedunculated, 29 sessile) contained adenocarcinoma. Carcinoma in situ was found in 15 polyps; invasive carcinoma, defined as infiltration of carcinoma cells below the level of the muscularis mucosae and into the submucosa, in 30 (malignant polyps). 8 pts with carcinoma in situ were treated with endoscopic polypectomy alone, six underwent colorectal resection; no residual tumour was found in all the surgical specimens. None of these had adverse outcome. 24 pts with invasive carcinoma (6 pedunculated, 18 sessile), underwent additional bowel resection after polypectomy. No residual carcinoma was found in the resected bowel specimens except in one case. The remaining 3 pts did not undergo surgery because of critical performance status and advanced age; 3 refused surgery. Staging was defined according to Astler and Collier classification, as Dukes A in 21 pts, B1 in 1, C1 in 2 pts. There was no operative mortality, the rate of unrelated morbidity was minimal. 2 pts in stage C1 with sessile malignant polyps died with metastatic disease 24 and 32 months postop, respectively. In 5/45 pts (11.1%) yearly endoscopic control examination after surgical or endoscopic resection revealed recurrent pathological findings suitable of endoscopic excision (polyps <1cm diameter). **Discussion.** Our treatment is guided by the consideration that cancers showing submucosal invasion gain access to lymphatic diffusion with 15-36% risk of lymphnode metastasis as described in the literature. We generally favour definitive bowel resection in case of malignant polyps, unless the increased risk of recurrence is offset by age related limited life expectancy and substantial comorbidities. **Conclusions.** Resection is needed in all cases of malignant polyps until additional data will show whether lymphatic or vascular invasion is associated with a significantly higher risk of adverse outcome. Although based on small numbers, our study confirms the need for yearly endoscopic controls, a three-years interval could be considered sufficient in preventing CRC.

# PREOPERATIVE RADIOCHEMOTHERAPY IN RECTAL CANCER

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**INTRODUCTION** This study was undertaken to investigate down-staging effects after preoperative radio-chemo-therapy on rectal cancer.

**MATERIALS AND METHODS** Between 1992 and 1998, we observed 39 patients with a histologically proven adenocarcinoma. All the patients had the same clinical investigation standard. The study cut off: age over 80 years; Karnofsky's performance status under 80, pregressed pelvic irradiation,

T1-2, M1 cancer. We identified 21 eligible patients, 15 males and 6 females, median age 65.5 years (range 38-77), who received the treatment. The pretreatment staging was: 4 T3N0M0; 11 T3N1M0; 4 T3N2M0; 2 T4N2M0. In 18 cases the adenocarcinoma histologic grade was moderately differentiated (G2). Patients have been treated with a three-field technique and received a 45 Gy total dose in conventional fractions. Chemotherapy with 5FU 350 mg/mq/die and Folinic acid 10 mg/mq/die during the first and the fifth week of RT.

**RESULTS** All patient underwent surgery. In all cases has been observed a downstaging and in 24% of cases had a complete pathologic response to pre-operative therapy, with no tumor found in the specimen: 5 cases (24%) T0N0M0, 5 cases (24%) T2N0M0, 9 cases (42.5%) T2N1M0, 2 cases (9.5%) T3N1M0. During post-operative period we observed 1 pelvic abscess and 2 anastomotic fistulas.

**DISCUSSION** This treatment produces a considerable tumor downstaging histologically confirmed. We did not observe a significant increase of perioperative complications.

# GROWTH FRACTION MEASURE AS PROGNOSTIC FACTOR IN ANAL CANAL CARCINOMA

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# INTRODUCTION

Ki-67 is a murine monoclonal antibody that binds to a nuclear antigen expressed in all stages of the cellular cycle except G0 (1). Thus Ki-67 immunostaining can be used to measure growth fraction of the neoplasms. The purpose of this study is to examine the relationship between Ki-67 score and prognosis in anal canal carcinoma.

# MATERIALS AND METHODS

Between January 1989 and June 1997 we evaluated 18 patients affected by cloacogenic or squamocellular anal canal carcinoma. Six patients underwent abdominoperineal resection, followed by radiochemotherapy in 4 cases. Two patients underwent local excision. Seven patients underwent chemoradiotherapy followed by local excision. Mean follow-up time was 5.3 years (range 18 months-9 years). Five (m sections of tissue were tested with monoclonal anti-Ki-67 antibody (MIB-1, DBA, Milano Italy). Nuclei staining with any intensity for MIB-1 were considered as positive. A Ki-67 score was defined as the number of tumor cells with positive nuclear immunostaining divided by the total number of tumor cells counted per section. Ki-67 score was considered low in the range 0%-20%, medium in the range 21%-40% and high if greater than 40%. Pearson's (2 test was employed to test for association between Ki-67 score and prognosis. Difference was considered significant at  $p < 0.05$ .

# RESULTS

Ki-67 score ranged from 32% to 45% in individual tumors (mean 37.5%). Ki-67 score was higher than 40% in 4 patients: 3 of them showed relapsing tumor and 1 was disease free. Ki-67 score was lower than 40% in 14 patients: 7 of them showed relapsing tumor and 7 were disease free. No correlation was found between neoplastic relapse and Ki-67 score higher than 40%.

# CONCLUSION

The fact that Ki-67 cannot measure time in cell cycle could be responsible for the apparent lack of correlation between growth fraction and biologic behavior. Additional prognostic factors should be examined.

# REFERENCE

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# **LOCAL EXCISION OF RECTAL TUMOURS WITH TRANSANAL ENDOSCOPIC MICROSURGERY (TEM)**

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**Introduction:** Transanal endoscopic microsurgery (TEM) is a novel technique, first introduced by Buess and coworkers in 1983 for the treatment of large sessile polyps of the rectum. Due to the excellent results, the indication was then extended also for the removal of low risk early adenocarcinomas (pT1, G1-G2).

**Methods:** Between January 1992 and April 1998, 17 patients underwent TEM resection of rectal tumours at our Department. The median age was 64 years (range 48-70). Ten patients were males and seven were females. All patients underwent rectoscopy with biopsy, colonoscopy, endorectal ultrasound, and addominal and pelvic TC. Indications for the 17 patients submitted to TEM were 12 villous adenomas and 5 T1 adenocarcinomas. Villous adenomas ranged from 3.2 to 5.0 cm in size (mean 4.5 cm), and T1 adenocarcinomas ranged from 2.4 to 3.0 cm (mean 2.8 cm). Resection was performed using the mucosectomy method in one patients with villous adenoma of the extraperitoneal rectum, partial-wall excision in two patients with villous adenomas of the intraperitoneal rectum and full-thickness excision in fourteen patients; nine patients for villous adenomas of the extraperitoneal rectum and five patients for adenocarcinomas T1(G1-G2) of the extraperitoneal rectum.

**Results:** All tumours were removed radically and in none was there tumour involvement of the resection margin. Distal extent of tumors ranged from 6 to 15 cm from the anal verge. The operative time ranged from 120 to 220 minutes (mean 180 min). Estimated blood loss ranged from 0 to 450 cc (mean 200 cc). In no case was conversion to conventional method of resection necessary at the time of the TEM resection. Complications occurred in one patient: anastomotic leakage of the extraperitoneal suture with abscess drained in the rectum. Functional results were excellent; none of the patient had developed incontinence. A radical rectal resection as a second step was performed in 1 patient for advanced carcinoma in the histologic examination of the specimen. The mean length of hospital stay was seven days (range 3-14). The median follow up was 28 months (range 8-62). To date, no patient had local or distant recurrence.

**Conclusion:** These initial results compare well with those of earlier reports, indicating that the TEM has a useful place in the management of sessile adenomas of the mid and upper of the rectum, and of some carefully selected carcinomas. The advantages of TEM are less or no postoperative pain, unrestricted morbidity, short hospitalization, quick rehabilitation and absence of skin scars.

## **Early Gastric Cancer : follow up of 412 patients.**

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**Introduction:** the authors investigated the follow-up of 412 patients with EGCooperated on in the authors unit from 1976 to 1994 (25,7% of 1600patients resected for gastric cancer).

**Methods:** all patients were submitted to a subtotal or total gastrectomy with

lymphadenectomy of the I' and II'level (in the definition of JRS GC). The microscopic types were classified according to Lauren's and Kodama's classification. The mean follow up was 9 years (range 1-22 years)

**Results:** the survival rates at 5 and 10 years were 91,8% and 88.9%. The infiltration of the wall, Kodama types, size of the tumor, and lymph node status, were correlated significantly with survival. The bivariate analysis showed that the survival rate for N+ sub mucosal type patient group was 74.8% after 5 years and the survival rate for N+ PenA type patient group was 61.2% after 5 years (p= 0.0001). Cox Wilcoxon's test showed a stronger significative role of the PenA type in predicting an aggressive course of the disease, than the lymph node status.

**Conclusion:** Kodama's classification identify a high risk sub-group of patients. In our opinion this sub-group had to be considered as affected by advanced cancer from the prognostic and therapeutic point of view.

## **Combined intraperitoneal chemotherapy and surgery in peritoneal carcinomatosis.**

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The discouraging experience in the treatment of peritoneal carcinomatosis from colon cancer and the high frequency of advanced stages in diagnosing ovarian cancer give place in the past to several methods of therapeutic approach. Intraperitoneal chemotherapy was not used in colon cancer whilst in ovarian cancer is currently used in a separated fashion after the surgery at the moment of the presenting carcinosis. This attitude involves same drawbacks namely, of course, at first to leave untreated the micrometastasis that are present at the moment of the first operation in advanced ovarian cancer, to leave undisturbed the growth of intrabdominal adhesences that will impede the freely circulation of the peritoneal lavage with chemotherapeutic agents, and finally to leave the inflammation cells free to produce their "growth factors" that in turn help the neoplastic growth ("cell entrapment hypothesis"). According to Sugarbaker we have applied the procedure to patients up to seventy five years old, with peritoneal carcinosis from colon cancer, with advanced stage of ovarian cancer (stage III-IV) without liver and retroperitoneal metastasis. Cytoreductive surgery implies isteroannessicectomy, appendectomy, omentectomy, splenectomy, resection of the pelvic, lateral and peritoneum of hypocondria. In some patients we performed a sleeve resection of the sigma. All the neoplastic growths scattered on the surface of the peritoneum were thoroughly removed. At this point we put in place three drainage tubes plus a Tenckhoff catheter and started thorough lavage of peritoneal cavity to obtain the clearance of fibrin products. After twenty-four hours we began the intraperitoneal chemotherapy with Mitomicine-c, 5-FU, Cisplatin, according to the type of the tumor. It is possible to attain high concentrations of chemotherapy without systemic complications. The protocol implies three following cycles of intraperitoneal chemotherapy in the next three months. We have treated eleven patients ranging the age between forty and seventy-five, women, five with colon cancer and six with ovarian cancer. The results were better in ovarian cancer from the point of view of survival for the type of implantation of the metastasis in this kind of tumor. Therefore performance status of these patients was sensibly better regarding the very short span of life in these patients if untreated. Some drawbacks present in this procedure, the magnitude of the surgical operation, the risk of the infection in the management of the catheter of Tenckhoff for several months, the risk of dehiscence in presence of intestinal anastomosis made it fit for these patients in whom no other therapies are available, bearing in mind that the systemic chemotherapy it is not precluded anyway.

P.H. Sugarbaker: Peritonectomy procedures. Ann. Surg. Vol. 221, N. 1-1995.



# LOCAL RECURRENCE FOLLOWING RADICAL SURGERY FOR COLORECTAL CANCER

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Local recurrence of colorectal cancer after curative surgery is a major clinical problem. Aim of our study was to present our experience in treating such patients and present the results of our efforts.

Between 1991 and 1998, 325 patients underwent resection for colorectal cancer in our Department. Thirty-three out of them had local recurrence within first two years. Most of the 33 patients had Dukes' stage B (n:15) and stage C (n:15) tumors, which were located mainly in rectum (n:16) and sigmoid colon (n:13). The incidence of local recurrence is 12% for tumors staged Dukes' B and C. All patients with a primary tumor classified as Dukes' C received adjuvant chemo-radiotherapy, while only a part of the patients with a Dukes' B tumor received such treatment. The operations were performed by many surgeons with various experience and technique. The distal margin of recurrent rectal cancer was (3 cm).

Nineteen out of 33 patients received palliative treatment and 17 of them died within 7 months. The remainder 14 underwent radical excision of the recurrent tumor: 6 out of 14 patients died within 2 years and 8 are still alive after 4 to 30 months.

The only hope for long term survival for the patients presenting with local recurrence from colorectal cancer after radical treatment of their primary tumor is when the local recurrence is identified at an early stage and treated in an aggressive manner, possibly with radical excisional surgery with clear surgical margins. Therefore intensive postoperative follow up of colorectal cancer patients (with newer techniques when necessary) is significant to identify occult or early local recurrence.

## ADJUVANT THERAPY FOR RADICALLY RESECTED PANCREATIC CANCER

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**Introduction:** despite large therapeutic efforts to increase survival after pancreatic cancer resection, recent results are generally unsatisfactory. It is not clear if adjuvant therapy, as chemotherapy with or without radiotherapy, prolongs survival or improves quality of life of pancreatic cancer resected patients. Specific objective of this study was to define if adjuvant therapy may give a benefit on long-term survival in resected pancreatic carcinoma.

**Methods:** we observed 58 consecutive cases of pancreatic neoplasm from June '94 to June '98. 20 of them (34,5%) underwent curative resective surgery, 21 (36,2%) endoscopic or surgical palliation and 17 (29,3%) palliative medical care.

**Results:** in resected group, 17 cases suffered from pancreatic ductal carcinoma (PDC) and UICC-JPS postoperative staging was: stage I 2-1; stage II 5-4; stage III 6-6; stage IV 2-4. In 4 of 15 patients chemoradiotherapy (CRT) with ECF schedule and conformal technique was performed in an adjuvant setting. PCD operative mortality rate was 11,8% (2 patients), overall survival was  $13,0 \pm 10,7$  mo (median 12,8 mo) and 1 and 2 year survival rate was 53,3% and 42,9% respectively. Stratifying in 2 groups, CRT+ and CRT-survival was  $27,5 \pm 6,8$  mo (median 27,1 mo) and  $10,1 \pm 6,4$  mo (median 9,5 mo) respectively. 1 and 2 year survival rate was 100% and 100% in CRT+ group and 44,4% and 27,3% in CRT- group. Stage-related survival analysis is reported in the table (results in months):

Stage	UICC			JPS		
	PDCs (no pts)	CRT+ (no pts)	CRT- (no pts)	PDCs (no pts)	CRT+ (no pts)	CRT- (no pts)
I	16,9 (2)	0	16,9 (2)	12,8 (1)	0	12,8 (1)
II	11,3 (5)	27,5 (1)	7,3 (4)	15,7 (4)	0	15,7 (4)
III	14,9 (6)	23,2 (2)	10,8 (4)	13,5 (6)	27,1 (2)	6,7 (4)
IV	20,6 (2)	36,3 (1)	4,8 (1)	16,1 (4)	28,0 (2)	4,3 (2)

**Discussion and conclusions:** although these preliminary data do not support conclusive evidence, they suggest that an aggressive adjuvant therapy combining chemo and radiotherapy may give a benefit in prolonging survival of case of radically resected pancreatic cancer.

## THE HEREDITARY CANCER OF THE COLON-RECTUM: GENETICS AND SURGICAL PROBLEMS

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**Introduction** The hereditary cancer of the colon-rectum without polyposis is a dominant autosomal hereditary disease. It defers from the sporadic cancer for the premature age of insorgence (mean age 44 years) the location in the right colon (60-70%) and the particular incidence of synchronous and metachronous malignancies of the large intestine. The diagnosis is performed on the basis of the clinical history of the patient and his familiar history; the Minimum Amsterdam Criteria (MAC - 8/1990) are the contemporary presence of the following conditions: 1) cancer of the colon-rectum histologically confirmed in at least three members of one same family of which at least one member in relationship of the first degree with the others two; the 2) affected subjects must belong at least two generations 3) at least one of the affected subjects must have an age lower than 45 years at the diagnosis. **Methods** From the series of our Institute (1970-1996) we selected 32 subjects operated for cancer of the right colon and with an age lower than 50: only four have a positive familiar anamnesis according to MAC. Two patients were males; the mean age was 42 yrs (range 27-48). All the patients had an hepatic flexure cancer without dissemination to nodes and no metastases. **Results** In all patients a right hemicolectomy was performed. In the genetic analysis we searched for the instability of some polymorphous microsatellites localized on various chromosomes in the tumoural tissue and in the peritumoural normal tissue. The molecular analysis was directed to microsatellites CD4-FABp2-VNTRp53-DRPLA-SAT: in fact they have an instability in other malignancies. At today all the patients are alive. The genetic analysis were negative in all the cases. So it was possible to perform a clinical diagnosis of hereditary cancer of the colon-rectum without polyposis. However it is important to search for genetic anomalies. **Conclusions** Up today therefore it is fundamental an accurate familiar anamnesis and to evaluate the age of insorgence of the tumor: they represent the more important markers of the disease. In the surgical therapy we choose a conservative treatment performing limited resections: this attitude seems to be justified from the reduced risk of these patients to develop a second tumour in another portion of the colon-rectum. Finally the hereditary cancer of the colon-rectum without polyposis seems to have better prognosis compared with the sporadic cancer of the colon-rectum.

### Glutamine in the chemoprophylaxis of acute and subacute actinic enteritis by preoperative radiotherapy in patients affected by rectal cancer .

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**Introduction.** Glutamine is a non essential aminoacid which carries out several important metabolic functions among which we put in evidence the capacity to preserve the integrity of the intestinal wall. The need of glutamine increases more when the intestinal mucosa is suffering for radio and/or chemotherapeutic treatments. For these reasons an integration of TPN with glutamine, normally absent in standard TPN, can result particularly useful in preventing damages on the intestinal mucosa. The aim of this study is to evaluate if parenteral supplementation of glutamine can decrease damages caused by preoperative radiochemiotherapy on the intestinal mucosa, improving bioumoral rate of catabolism and reducing symptoms due to the drug toxicity and actinic enteritis.

**Materials and Methods.** 60 patients with rectal cancer were included in this study. They all received radiotherapy combined to chemiosensibilization (5FU), followed by resection (protocol of Istituto dei Tumori di Napoli for rectal cancer). A total of 4680 Grey, in two daily administrations for 13 days was given. Each session was preceded by infusion of 5FU, 150 mg/mq iv. The patients were divided in two groups of 30 each. First group received 1g/1 per kg/weight single dose iv. per central line (Glamin - Pharmacia & Upjohn; 500 mL/d) daily during all the radiochemical treatment. The other group did not receive any supplementation.

**Results.** No patient of the study or control group had to withdrawn radiochemiotherapeutic treatment for pharmacological intolerance or for any other cause.

No significative alterations of normal values were seen neither absolutely nor between two groups, with the exclusion of a decrease of WBC in 9 cases (30%) and in particular of neutrophils in the control group. This leukopenia was not so severe to determine preoperative treatment interruption. As regards the control group 43% (13/30) complained of tenesmus, 56% (17/30) diarrhoea and 70% (21/30) abdominal pain. On the contrary, in the glutamine-treated group, 13% (4/30) referred tenesmus, 30% (9/30) diarrhoea and 23% (7/30) abdominal pain. It must be underlined that drugs used to treat medical complications were more successful in the glutamine group (100%) than in the control group (60%). One more significative data was reported by histopathological exam of biopsies on inflamed mucosa and random on apparently healthy mucosa in both groups. In the control group 23% (7/30) showed slight phlogistic infiltrate, 46% (14/30) moderate infiltrate, 30% (9/30) severe infiltrate. In the glutamine group 13.5% (4/30) did not show any phlogosis, 86.5% (26/30) a slight phlogistic infiltrate.

**Discussion and conclusions.** Basing on this data, the action of glutamine in association to chemioradiant preoperative treatment can be positively recognised. Glutamine protects the integrity of intestinal mucosa from chemotherapy and reduces phlogosis induced by radiotherapy. Our hope is to achieve the same positive results by oral administration of glutamine.

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## Surgical Oncology (Session 2)

### CDDP HEPATIC ARTERIAL INFUSION (HAI) AND I.V. 5-FU CHEMOTHERAPY FOR UNRESECTABLE COLORECTAL LIVER METASTASES.

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**INTRODUCTION:** The aim of the present study was to evaluate the effectiveness of the combination CDDP HAI and bolus i.v. 5-FU in terms of response and survival rates in colorectal liver metastases.

**METHODS:** One hundred-twenty-three patients at stage II and III according to Gennary's classification were included in a phase II randomized multicentric clinical trial. All the cases were randomized in two different modalities to receive CDDP (bolus vs. chronic HAI) 24 mg/m<sup>2</sup>/day and bolus i.v. 5-FU 500 mg/m<sup>2</sup>/day both per 5 every 28 days.

**RESULTS:** Out of 98 evaluable patients objective responses were 51 (52%) with no significant differences between the two groups. Complete responders were 17 (17.3%). As far as toxicity regarded, haematological events and nausea/vomiting were the most observed ones (53% and 79%, respectively) but only 26.4% and 30.4% were G>3 events. Minor toxicity were pain, gastrointestinal, fever and neurological peripheral (ranging from 15% to 26%). Group B (CDDP chronic infusion) experienced a lower number of toxic events in comparison with group A (157 vs. 120). The 5-year overall survival was 19%, without statistical difference between the two Groups. Complete and partial responders displayed a longer survival than patients with stable or progressing disease (25% vs. 0% at 5 years, p=.002).

**CONCLUSIONS:** The response and survival rates were satisfactory even if the toxicity was relatively high, affecting the quality of life. Particularly, the complete responders had a long-term survival, which is unusual in patients with unresectable colorectal liver metastases.

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### MELANOMA OF THE GLANS PENIS: THERAPEUTICAL DECISIONS.

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**Introduction:** penile melanoma (PM) is rare; it is not clear whether this site of disease presentation should be evaluated as a separate clinic-pathologic entity from the reminder of cutaneous melanomas (CM). **Case description:** we describe a rare presentation of PM in which 3 successive primaries arising from an area of melanosis on the glans penis and prepuce were operated (15 and 5 years before elsewhere). The management of this lesion consisted of amputation of the shaft of the penis to its mid third together with a wider skin excision. The melanoma was 1.45 mm deep and ulcerated. Prepuce and balano-prepuce ridges showed multiple foci of in situ or minimally invasive melanoma which were present in decreasing quantities from the site of the main tumor to the periphery, in continuity with a diffused benign melanosis. No sentinel node biopsy was proposed as at that stage we were considering this diagnostic procedure only for lesions thicker than 1.5 mm. The patient unfortunately developed left-sided groin metastases eight months after the penile operation and six months after the groin dissection, during an adjuvant Interferon treatment, he developed distant metastases. Fourteen months later the patient died of progressive disease. **Conclusion:** melanosis is a histologically benign lesion and the pathological pattern described in this patient was more akin to a melanosis than to a penile lentigo, where melanocytes are characterized by some degree of atypia. Reliable and objective criteria for differentiating such borderline skin lesions have not been clearly established and there is no generalized agreement on the biological and clinical implications of these lesions. When diffuse melanotic areas are present in the genital region, in particular given the reluctance of patients to present with such skin lesions, the index of suspicion should be high and an aggressive follow-up policy advocated. Treatment guidelines should not significantly differ from the usual approach of CM.

# **HEPATIC RESECTION FOR LIVER METASTASES AFTER PERCUTANEOUS TRANSAXILLARY INTRA-ARTERIAL HEPATIC CHEMOTHERAPY (IAHC)**

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**Introduction.** Hepatic resection is the most effective treatment for liver metastases from colorectal cancer. Failures to achieve a curative hepatectomy depend on technically unresectable or large or multiple metastases. Moreover, an intentional curative resection is often frustrated by the progression of unrecognized hepatic micrometastases becoming evident shortly after the primary resection. Intra-Arterial Hepatic Chemotherapy (IAHC) has been demonstrated to provide higher response rates than systemic treatments and might represent an effective neoadjuvant treatment to improve the results of subsequent hepatic resection. The authors present the results of hepatic resections in selected cases among a clinical series treated by percutaneous transaxillary IAHC (1, 2) for liver metastases from colorectal cancer.

**Materials and Methods.** Enrollment criteria to the percutaneous IAHC include: 1) hepatic metachronous metastases from colorectal cancer without extrahepatic disease; 2) good performance status; 3) informed consent. A 6 F polyurethane catheter is implanted percutaneously in the hepatic artery and connected to a self-sealing silicone reservoir (Port-a-Cath, SIMS Deltec) that is surgically placed in a subcutaneous pocket on the upper left chest wall. Chemotherapy based on continuous infusion of fluorodeoxyuridine (FUdR - dose escalation 0.15-0.30 mg/kg/day for 14 days every 28 days) and dexametasone (28 mg) is started 7 days after the procedure using external infusion pump (CADD-1, SIMS Deltec) connected to the port. Total body spiral CT-scan is performed to re-stage the disease every 3 cycles of therapy. As for the response to the therapy, patients (Pts) are classified as Progressing Disease (PD), Stable Disease (SD), Partial Responders (PR), and Complete Responders (CR). **Results.** Between december '96 and december '98, 32 Pts, aged between 37 and 73 years, were enrolled in the study for IAHC. Response to the treatment was evaluated in 30 Pts; 2 cases were not considered because of performed cycles less than 3, due the recurrent displacement of the catheter. Over a mean treatment period of 8±4 months (range 1-11 months), 4±6 FUdR cycles/Pt (range 3-10 cycle/Pt) were administered. PD, SD, PR, and CR were recorded in 5 Pts (17%), 10 Pts (33%), 13 Pts (43%), and 2 Pts (7%) respectively, with an overall response rate (PR+CR) of 50%. Out of the 13 PR, 7 Pts (54% of PR, 23% of all cases) underwent surgical resection, including 2 right hepatectomies and 5 segmentectomies. Perioperative mortality occurred in 1 case (pulmonary embolism). No perioperative morbidity was recorded. During the follow up period (range 5-13 months, median 7±4 months) hepatic tumor relapse was recorded in 1 case, while 5 Pts are disease-free. **Conclusions.** IAHC by a percutaneous transaxillary intra-arterial device may represent an effective neoadjuvant treatment for metastatic liver disease and improve the results of subsequent hepatic resections.

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# **SENTINEL NODE BIOPSY FOR MALIGNANT MELANOMA**

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**INTRODUCTION.** The effectiveness of prophylactic lymphadenectomy in the therapy of intermediate thickness melanomas is controversial. Sentinel node biopsy has been introduced by Morton (1992) to diagnose early metastasis and to identify patients who are likely to benefit from lymphadenectomy.

**METHODS.** One hundred fifty two patients with melanomas of intermediate thickness (I-II clinical stage of disease, T<sub>2-3a,3b</sub>, N<sub>0</sub>, M<sub>0</sub>) underwent sent node biopsy between March 1996 and January 1999 at the Plastic Surgery Department of the Istituto Dermopatico dell'Immacolata of Rome. The sent nodes were identified through a vital dye ((Patent Blau), preoperative and intraoperative lymphoscintigraphy.

**RESULTS.** Incidence rate of micrometastasis in the sent nodes has been found largely dependent on the thickness of the primary lesion (T<sub>2</sub> : 6,2%; T<sub>3a</sub>:14,6%; T<sub>3b</sub>: 25.0%). Patients with positive sent node biopsy underwent a radical lymphadenectomy. Further metastasis in other nodes were found mainly in patients with primary lesions thicker than 3 mm. Sent nodes has been successfully identified in 91% of the patients using vital dye and preoperative lymphoscintigraphy and in 100% using vital dye associated to intraoperative lymphoscintigraphy. When sent node has not been identified a prophylactic radical lymphadenectomy has been performed. In our experience false negative rate has been 1,9%.

**DISCUSSION AND CONCLUSIONS.** Sentinel node biopsy undoubtedly has a staging value for intermediate thickness melanomas as the evidence of micrometastasis modifies the clinical stage and the prognosis of the disease. The actual trends in sent node harvesting include intraoperative lymphoscintigraphy associated to vital dye perilesionally injected. The identification of sent node using vital dye alone could be considered even if less effective, more complex and more time consuming. Surgical approaches in harvesting the sent nodes, with or without intraoperative lymphoscintigraphy, are also presented and discussed.

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# **Hepatocellular carcinomas in cirrhotics: selection criteria for surgical resection and early results.**

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**Introduction.** Surgical resection is the most effective therapy for hepatocellular carcinoma (HCC) in patients with cirrhosis both in terms of early and late results. At the moment of the diagnosis about 20% of HCC's in cirrhotic liver are suitable for surgical treatment. This number of patients emerge from an oncologic evaluation, obtained by the study of the parameters tumor (T), lymphnodes (N) and metastasis (M), combined with the definition of the functional status of the liver. Liver ultrasound, spiral CT and dynamic RNM define the T parameter; visceral angiography with lipiodol (LUF), followed by a CT scan without contrast 10-15 days later, are performed to exclude multicentricity. Videolaparoscopy (VLS) and intraoperative ultrasound are the last diagnostic steps and the first therapeutic. Whole body CT scan provides the parameter M evaluation. Although several methods of liver function evaluation have been proposed, the most diffuse system and so the most valuable for large numbers is the Child-Pugh classification.

**Methods.** Between January 1990 and July 1998, out of 491 patients presented at our Department with a focal pathology of the liver, 259 were HCC's in cirrhotic livers and 35 (13,5%) of these underwent a surgical resection. All patients, 27 men and 8 women, were classified as Child Pugh A. Fifteen major resections, 15 minor resections and 5 enucleoresections were performed.

**Results.** Eight major postoperative complications (4 bleeding, 2 sepsis and 2 liver failure) and 28 minor (24 pleural effusions and 4 resistant ascites) were observed. In four patients a re-operation was necessary to stop the postoperative bleeding and three died for a coagulopathy (DIC). The two sepsis were due to a subphrenic collection and were treated by percutaneous drainage CT-guided. The two ascites were cured with conservative therapy (TPN and diuretics).

**Conclusions.** Careful preoperative selection of the cirrhotic patients with HCC who are candidates to surgical resection is mandatory. In this way, as demonstrated by our experience and according to the literature, early good results are preventable.

### The use of the A.B.B.I. device in the management of non palpable breast lesions: preliminary results

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In the last twenty years early detection by mammographic screening has impacted upon the local control and cure of breast cancer. Randomized studies, in fact, identified a 30% reduction in mortality for women enrolled in mammography screening programs. Despite these favourable results, still today clinical management of Non Palpable Breast Lesions (NPBL) can be difficult. Fine-needle biopsy results often inadequate and for a large number of patients surgical excision is mandatory. The introduction of the Advanced Breast Biopsy Instrumentation (A.B.B.I.) system for the diagnosis of NPBL allowed to obtain a certain histologically proven diagnosis in close to 100% of the cases. In many patients surgical biopsy can be therefore avoided with reduction of economical and psychological costs. We report a preliminary series of 236 consecutive patients who underwent A.B.B.I. procedure. This is a x-ray digital system with a mechanical arm guided by computer targeting, able to drive a needle-biopsy or to remove the entire suspect area (if smaller than 2 cm) through a special rotating device. In the last ten months, 236 patients affected by NPBL underwent A.B.B.I. procedure at our Institutions. In 83 patients (35.2%) an excisional biopsy was performed: 41 nodules, 33 microcalcifications, 7 nodules with microcalcifications, and 2 parenchymal distortions were removed. In the remaining 153 cases (64.8%) a multiple core-biopsy was performed in 88 nodules, 30 microcalcifications, 22 nodules with microcalcifications and 13 parenchymal distortions. Excisional and core biopsies were performed in a mean time of 45 (35-70) and 25 (15-50) minutes respectively. Histological samplers showed the presence of a malignant lesion in 27 (32.5%) excisional and 49 (32.1%) core biopsies. Mortality and major morbidity were absent. Minor morbidity consisted of one case of haematoma in a trombocytopenic patient (0.4%). A.B.B.I. system is a safe, cost-effective, mini-invasive procedure that allows excellent cosmetic results. Moreover, in the presence of benign lesions (more than 65% in our experience), it is also a one-step and one-day procedure that avoids large surgical excision and parenchymal alterations often causing radiological artifacts at the following mammographic controls. Finally, our experience confirms that the use of A.B.B.I. system determines an improvement of the patients' satisfaction and the presence of significant economical benefits.

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### SELECTIVE RADIO-GUIDED SURGERY OF CLINICALLY OCCULT BREAST LESIONS

O. Buonomo, A. Cabassi<sup>#</sup>, A. Felici, G. Pernazza<sup>#</sup>, A. Santellocco, S. Servetti, G. Atzei<sup>§</sup>, E. Cossu<sup>°</sup>, Mn. Guazzaroni<sup>°</sup>, A. Mauriello<sup>^</sup>, A. Piazza\*, M. Roselli. Clinica Chirurgica Università "Tor Vergata" Roma, <sup>#</sup>Chirurgia Oncologica ASL5 Roma, <sup>§</sup>Servizio di Medicina Nucleare ASL5 Roma, <sup>°</sup>Istituto di Radiologia Università "Tor Vergata" Roma, <sup>^</sup>Istituto di Anatomia Patologica Università "Tor Vergata" Roma, \*Istituto di Tipizzazione Tissutale CNR Roma. The surgical management of occult breast lesions presents two orders of clinical problems: a) the exact preoperative and intraoperative localization of any intramammary lesion, and b) the extension of the axillary lymph node dissection for those lesions resulted to be malignant. As far as the first problem is concerned, many techniques have been described, *i. e.* : skin markers; straight needle; hookwires needle; dye injection; and sonographic centering. Concerning the extension of axillary lymphadenectomy, different possibilities

to minimize the surgical approach in early breast carcinomas have been proposed, *i. e.* : single lymph node sampling; only I or I and II level dissection; and, more recently, the Sentinel Node (SLN) biopsy. The aim of this study was to evaluate the feasibility to correctly identify and remove during surgery, by intralesional injection of a radiotracer (Nanocoll, Amersham-Sorin) with the aid of a hand held  $\gamma$ -detecting probe, any unpalpable breast lesion. Out of 53 cases, 34 invasive carcinomas (T1a,b,c) were found as well as 18 intraductal carcinomas and 1 fibroadenoma. At surgery, breast lesion radiolocalization was extremely easy in all patients, due to the lesion/background count ratio higher than 10:1, even 24 hours after injection. For those carcinomas (n.34), with an invasive component by frozen section examination, SLN biopsy was also performed at the same time. In the present study (validation-study), SLN eradication was followed by a complete axillary dissection for appropriate node staging. In 27 out of 34 patients bearing invasive carcinomas, the SLN was easily identified (SLN/non-SLN radioactive ratio >2:1). SLN accurately predicted axillary lymph node status in 100% of the T1 carcinoma patients. Thus, selective radioguided surgery appears an easy and reliable procedure to locate and eradicate both benign and malignant breast lesions along with SLN.

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### SURGICAL TREATMENT OF HILAR CHOLANGIOCARCINOMA: PERSONAL EXPERIENCE

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**Introduction.** Hilar cholangiocarcinomas or Klatskin tumors are rare tumors with poor prognosis. Surgical resection provide a good palliation in most patients and may be curative in some. Our experience of aggressive surgical strategy is here reported.

**Methods.** Between January 1990 and September 1998, 25 patients affected by Klatskin tumor were observed. Fourteen of these (56%), eight men and six women (mean age 59 years), underwent an attempt to surgical resection. Presenting sign or symptom was jaundice in all cases. Preoperative diagnosis was based on liver ultrasound, spiral CT, percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangiopancreatography (ERCP) and, since 1996, MR-cholangiography. Visceral angiography was obtained in selected cases only. Six patients with serum bilirubin level higher than 10 mg/dl, three scheduled for liver resection and one with cholangitis underwent a preoperative biliary drainage. According to the Bismuth-Colerette classification, the patients were classified as: 7 Type I, 2 Type II, 2 Type IIIa and 3 Type IIIb. Twelve patients (85%) had curative resection: hilar resection only in 7 cases and combined with a partial hepatectomy in 5. A hepatoduodenal ligament lymphadenectomy extended up to celiac axis was always performed. Two patients had palliative biliary resection with surgical drainage.

**Results.** One patient died of liver failure after a right hepatectomy with associated portal vein resection (7,1%). Postoperative morbidity was 42%, with no need of re-operation. Positive lymphnodes were observed in 8 cases (58%) and perineural invasion in 10 (74%). In 13 patients the final pathologic examination showed a sclerosing adenocarcinoma and in 1 a papillary type (7%). Median survival in the patients who underwent a curative resection is 28 months, with an overall 3-years survival of 45%. One patient died after 9 months for a myocardial infarction. Of the patients who underwent a palliative resection, one died of recurrence 9 months after the operation and the other is alive 3 months after the operation, without jaundice.

**Conclusions.** Aggressive surgical resection can prolong patients' survival. Careful preoperative management requires a multidisciplinary approach. Preoperative biliary drainage is often mandatory in order to improve early surgical outcome as hepatic resection in order to obtain tumor-free margins and improve prognosis.



### Hepatic arterial infusion versus systemic chemotherapy for non resectable colo-rectal liver metastases.

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**Introduction.** Purpose of this study is the evaluation of hepatic arterial infusion vs systemic chemotherapy for non resectable colo-rectal liver metastases. **Methods.** 86 pts, 46 males and 40 females, age 28-75 years, PS=0-2, with measurable or evaluable unresectable hepatic metastases (H2-H3b as Gennari) from colon (53) or rectal (33) carcinoma were assigned to receive systemic q21Leucovorin (100 mg/m<sup>2</sup> i.v.)+5-FU (375 mg/m<sup>2</sup> i.v.) for 5 days, alone (arm A, 27 pts) or in combination with 3x10<sup>6</sup>Ux3 times/week of r- $\alpha$  or  $\beta$  interferon (arm B, 26 pts) or a hepatic arterial bolus infusion of 5-FU (1000 mg/day for 7 days, then weekly) via a Porth-A-Cath placed, by laparotomy, in the gastroduodenal artery with ligation of the right gastric artery (arm C, 33 pts). **Results.** Global response rate (CR+PR>50%) was 10.5% in the group treated with F.A.+5-FU, 26.0% in the group receiving the double modulation of 5-FU with F.A. and Interferon and 36.49% in the regional treated group. NCI grade 1-2 toxicity was represented by mucositis in 30% of patients receiving the systemic therapies, flu-like syndrome in the majority of those submitted to Interferon, hepatic toxicity (50%), abdominal pain (32%), biliary sclerosis (10%) and catheter displacement (5%) in the intrahepatic treated group. **Discussion and conclusions.** The loco-regional therapy offered higher percentages in complete remission and lower in progression than the systemic treatments with a statistically significant difference (p<0.05). Unfortunately this favourable activity does not correlate to a significant advantage in terms of survival: in the responder patients, in fact, both the double modulation of 5-FU and regional therapy are superior to Folic Acid-5-FU, but without difference between each other. This is not surprising because of the non systemic effect of hepatic infusion, so that many patients died of extrahepatic metastases. Our experience, even if limited, shows objective results practically the same as those reported in the literature and suggest that intraarterial chemotherapy may represent the first line treatment for unresectable liver metastases from colo-rectal carcinoma for the good compliance and quality of life, even if its impact on survival is not clearly superior when compared to the systemic modalities. Therefore it is necessary to consider economic questions, since the Italian hospital cost of drugs is £185,364 in the Folic Acid-5-FU group, £475,164 in the group associating r- $\alpha$ -interferon, £1,379,160 when  $\beta$ -interferon is used and only £23,152 in the intraarterial treated group, even if a one-off cost of about £1,500,000 must be added for the catheter and placement. At present, clear evidence is needed in order to consider the simultaneity or the sequence of the two modalities as a multifactorial approach.

### The sentinel node in breast cancer

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**Introduction.** We are witnessing a revolution in breast cancer surgery. In the first phase (1970–1985) several trials demonstrated no difference in survival between patients treated with mastectomy and breast conserving surgery for small tumors. In a very recent past, a second phase started, with the aim of eliminating axillary dissection in node negative patients using the technique of sentinel node. Axillary dissection remains the gold standard for staging in patients with breast cancer. However, risk of significant postoperative morbidity and the low incidence of lymphnode metastasis in patients with small tumors have raised questions about the need for procedure. **Methods.** Pathological examination of sentinel node, the first node which receives lymph from the primary tumor area, could predict the status of the rest of the nodes, eliminating axillary dissection if not metastatic. Axillary

lymphoscintigraphy, performed after the injection of Tc – labeled colloidal particles subdermally close to the tumor site, shows the sentinel node and a gamma ray detection probe allows the intraoperative identification. If the node is metastatic, then the axillary dissection is performed. **Results.** Our experience includes 13 cases, operated on in the period November - December 1998. Patients with multifocal disease and previous breast biopsy were excluded. After the identification of the sentinel node a complete axillary dissection was carried out. In the first two cases we were not able to identify any sentinel node. In two cases we identified, but did not perform the biopsy, an internal mammary and a supraclavicular node, with negative axillary nodes in both cases. In the nine remaining cases we successfully identified one or more ( up to 3 ) sentinel nodes in the axilla. In 5 cases sentinel node was negative and also the rest of the axillary nodes ( mean 24 examined nodes ) was negative. In the other 4 cases the sentinel node was positive and also others non sentinel nodes were positive ( mean 22 examined nodes ). **Conclusions.** In this very limited, training series, the predictive value of sentinel node seems confirmed. New goals of breast cancer surgical treatment are: 1) minimize surgery 2) maximize information 3) maximize local control.

### Color-Doppler sonography of breast nodules: diagnosis enhancement with echo-contrast agents

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**Introduction.** Several contrast agents have been recently developed to increase flow detection with color-Doppler sonography. We illustrate our preliminary experience in the evaluation of solid mammary nodules by using Doppler sonography with echo-contrast agents. **Methods.** We evaluated 9 patients with breast nodules showing physical and sonographic features suspected for malignancy. At surgery 6 proved to be ductal carcinomas, 1 lobular carcinoma, and 2 fibroadenomas. All were examined with state-of-art technique: AU5 equipment (Esate Biomedica, Italy), 10 MHz probe, setting for detection of slow flow. Basal study included real-time study, color and power Doppler sonography, spectral analysis. The contrast medium Levovist (Schering, Germany) was administered manually as a single injection (400 mg/mL, 0.5-1 mL/s). The study was repeated with the same setting. Retrospectively we evaluated: vascularization grade (absent, low, moderate, intense, very intense), presence and number of vascular poles, flow distribution (perinodular, intranodular, or both), vessel tortuosity (regular, irregular, very irregular), flow direction (uni- or bidirectional). **Results.** No subject experienced any adverse reaction. The echo-enhancing effect was prompt, constant, and evident. Both benign nodules showed absent flow on basal study; after echo-contrast injection 1 presented low perinodular vascularization with single pole, regular vessels, and unidirectional flow. Three of 6 malignant nodules has vascular signal on basal study with low flow in 2 and moderate flow in 1, detection of a single vascular pole in 3, perinodular pattern in 3 and diffuse pattern in 1, regular vessels in 1 and irregular in 3, unidirectional flow in 3 and bidirectional in 1; after contrast agent administration 6 nodules showed vascular signal (low in 1, moderate in 4, intense in 1) with single pole in 3 and multiple pole in 2, perinodular distribution in 2 and diffuse distribution in 4, regular vessels in 2 and irregular in 4, unidirectional flow in 3 and bidirectional in 3. **Conclusion.** Our preliminary data are interesting. Contrast-enhanced sonography is a safe and powerful technique, and, though a limited overlapping was found, benign and malignant lesions showed several different features that allowed their correct recognition. Contrast agent may increase operator's confidence in diagnosing a suspected or probably malignant nodule and consequently leading to aspiration or surgical removal. Doppler sonography is increasingly used in breast imaging and represents a necessary complement to real-time assessment of suspect nodules. Selective use of the eco-contrast agent, for example in case of absent flow on basal study, may be an additional possibility.

**Retroperitoneal big leiomyosarcoma: a case report**

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**INTRODUCTION**

Primary retroperitoneal tumors have an incidence of 2/100.000. Leiomyosarcomas represent about 10% of the total retroperitoneal tumors (1)

**METHODS**

C.A. is a 52 years old man that complains of back pain, abdominal enlargement and weakness, about for 1 year. At presentation he has a serious anaemia and an abdominal palpable mass. Ultrasonography and CT show an irregularly marginated, large abdominal mass with cystic central regions. At operation it is found a large retroperitoneal mass extended to all abdomen. Its isolation and removal are very difficult. Because of the infiltration the first loop of small intestine is resected with LL duodeno-duodenal anastomosis. The diameter and weight of the mass are cm 35 and Kg 6,000 respectively.

Histopathology reveals a leiomyosarcoma at low grade of malignancy.

**RESULTS**

The postoperative period is regular. Several transfusions and NPT are necessary. On the 17<sup>th</sup> postoperative day is discharged from the clinic. Actually the patient is well 50 days after surgical treatment.

**DISCUSSION**

The retroperitoneal leiomyosarcoma is rare mesenchymal tumor that occurs in the fourth to fifth decade. Haematological examinations, plain abdominal x-rays, ultrasonography, CT can provide invaluable informations for the diagnosis (2). Its mean diameter is cm 14,6, the mean weight is Kg 2,000. Transperitoneal excision "en bloc" is the main goal of management. Unfortunately, complete excision can be obtained in only about 75% of cases because of the infiltrative nature. The role of adjuvant therapy is unclear. If the tumor recurs, repeat excision should be attempted. The recurrence rate is about 60%, survival at 5 yr is 35% (1, 2).

**CONCLUSIONS**

In the case reported the follow up is very short. The patient will undergo to oncological counseling, periodical hematological examinations, ultrasonography every three months and CT every six.

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**FREEZE OR FRY: A COMPARISON OF CRYOABLATION AND RADIOFREQUENCY ABLATION FOR MALIGNANT LIVER TUMORS**

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**Objective:** In this study we compared the complication and early local recurrence rates in patients with unresectable malignant liver tumors treated with either cryoablation or radiofrequency ablation (RFA).

**Background:** The majority of patients with primary or metastatic malignancies confined to the liver are not candidates for resection because of tumor size, location, multi-focality, or inadequate functional hepatic reserve. Cryoablation has become a common treatment in select groups of these patients with unresectable liver tumors. However, hepatic cryoablation is associated with significant morbidity. RFA is a recently developed technique that destroys liver tumors *in situ* by localized application of heat.

**Patients and methods:** Patients with hepatic malignancies were entered into two consecutive prospective, nonrandomized trials. The liver tumors were treated intraoperatively with cryoablation or RFA. Intraoperative ultrasonography was used to guide placement of cryoprobes or RFA needles. All patients were followed post-operatively to assess complications, treatment response, and local recurrence of malignant disease.

**Results:** Cryoablation was performed on 88 tumors in 54 patients and RFA was used to treat 138 tumors in 92 patients. Treatment-related complications, including post-operative death, occurred in 22 of the 54 patients treated with cryoablation (40.7% complication rate). In contrast, there were no treatment-related deaths and only three complications after RFA (3.3% complication rate,  $P < 0.001$ ). With a median follow-up of 15 months in both patient groups, tumor has recurred in 3 of 138 lesions treated with RFA (2.2%), versus 12 of 88 tumors treated with cryoablation (13.6%,  $P < 0.01$ ).

**Conclusions:** RFA is a safe, well-tolerated treatment for patients with unresectable hepatic malignancies. This study indicates that complications occur much less frequently following RFA of liver tumors compared to cryoablation of liver tumors and early local tumor recurrence is infrequent following RFA.

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**SENTINEL NODE BIOPSY: THE BEST METHOD TO STAGE MELANOMA PATIENTS FOR ADJUVANT TRIALS.**

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**Introduction:** sentinel node biopsy (SNB) has been proposed to select patients with primary melanoma for therapeutic lymphadenectomy. We wanted to investigate the accuracy in staging primary melanoma patients and the best method to perform the procedure: patent blue dye (PBD) and/or gamma detection probe ( $\gamma$ DP). **Method:** we studied 90 patients with cutaneous melanoma and clinically negative lymph nodes. A preoperative lymphoscintigraphy (LYS) visualized 135 SNs in 105 basins. PBD was injected at the same site/s of the LYS immediately prior to the operation. When a blue node was intraoperatively identified, its radioactivity level was measured with the probe. In the absence of blue coloration, the  $\gamma$ DP was used to detect the SN. **Results:** the SN was identified in the regional draining basin during intraoperative lymphatic mapping using PBD in 78.52% and by handheld  $\gamma$ DP in 95.5%, while considering intraoperative mapping with PBD and  $\gamma$ DP, the SN was detected in 98.5% of the 135 SNs described with the preoperative LYS. In two patients the SN was not identified. Twenty-two patients (24.4%) had pathological positive SNs, indicating the need for regional lymphadenectomy and in 18 of these patients, only the SN was metastatic. No major complications were encountered. Nine patients recurred, 3 in the basin biopsied for negative SN, after a median follow-up of 420 days. **Conclusions:** from the technical point of view, we support the use of both PBD and  $\gamma$ DP because when the SN was found stained, the duration of the procedure was shorter than in absence of stained nodes (10.1 minutes versus 16.8 minutes,  $P$  value 0.0002, t. student 3.78). From the oncological point of view, this technique seems to offer a simple and reliable method of staging regional lymph nodes in melanoma patients and it helps to avoid unnecessary lymphadenectomies, obtaining a more accurate staging, which permits to accrue patients with similar disease characteristics in adjuvant trials.

**Synchronous MALT-type lymphoma and adenocarcinoma of the stomach in *Helicobacter pylori* infection: a case report.**

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**INTRODUCTION** The development of simultaneous primary gastric lymphoma and carcinoma is a rare event and a possible etiopathogenetic role for *Helicobacter pylori* (HP) has been differently postulated for both diseases.

**METHODS** We report a case of synchronous gastric adenocarcinoma and low grade mucosa-associated lymphoid tissue (MALT) lymphoma in a 47 year-old male patient with a 6 months history of active chronic gastritis and histopathologic evidence of HP infection, non responding to standard eradication treatment. Endoscopy revealed a large tumor mass in the gastric body; histologic findings of multiple biopsies preliminarily suggested the possible coexistence of an intestinal-type adenocarcinoma with a low-grade MALT lymphoma, nevertheless immunohistochemistry on these specimens did not confirm the diagnosis of lymphoma. Blood profile and bone marrow aspirate were also normal. Abdominal CT-scan showed a 3x2cm tumor with enlarged nodes from the perigastric area up to the left gastric artery station. According to our standard preoperative staging procedure a laparoscopic exploration was performed, confirming the presence of a locally advanced gastric tumor staged as T3 N1; an enlarged lymphnode along the greater curvature was removed for immediate pathologic examination which revealed metastasis of adenocarcinoma. According to our current protocol for locally advanced gastric carcinoma, the patient underwent two cycles of neoadjuvant EEP chemotherapy (etoposide, epirubicin, cis-platin). Restaging after 2 months revealed an objective clinical response, with radiologic evidence of both tumor and nodes regression and R0 total gastrectomy with D2-lymphoadenectomy was successfully performed. Pathology showed two distinct populations of cancer cells in the same tumor mass: a poorly differentiated intestinal-type adenocarcinoma coexisted with a nodular proliferation of small lymphocytes with follicular center cell-like (centrocyte) features; the presence of HP was clearly demonstrated in the same specimen. A total of 34 lymph nodes were removed: 21 were negative, 6 showed lymphomatous infiltration only and 7 were the site of combined metastatic carcinoma with marginal lymphomatous involvement; in 3 of these latter nodes, a scleroatrophic pattern with isolated carcinoma foci was observed, as already evidenced in other patients of our series undergoing neoadjuvant chemotherapy.

**DISCUSSION AND CONCLUSIONS** The diagnostic peculiarities of the case, the coexistence of HP infection, the presence of synchronous tumors that were both in advanced stage, the selective effect of induction chemotherapy on just one cellular line, all represent distinctive features of exceptionality.

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**RESECTION OF LIVER METASTASES FROM COLORECTAL CANCER**

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**Introduction:** metastases from colorectal cancer are frequently discovered in the liver. In 15-25% of patients synchronous liver metastases are found during preoperative evaluation or at laparotomy. Another 20-30% of patients is affected by metachronous lesions, usually diagnosed during postoperative follow-up <sup>(1)</sup>. Liver resection offers a curative chance, with an overall 5-year survival rate of 15-32% <sup>(2)</sup>. The Authors report their experience in liver resection over a ten years period.

**Materials and methods:** 46 patients affected by liver metastases from colorectal cancer were submitted to liver resection between June 1987 and May 1997 (27 men, 19 women; mean age 59ys., range 40-74 ys.). Five patients had synchronous metastases, 41 patients had metachronous metastases. All patients were evaluated by ultrasonography, CT scan, FNAB and intraoperative ultrasonography. As for the extent of resection, we performed 32 non-anatomical resections, one extended right lobectomy, 4 right lobectomies, 6 left lobectomies, 3 left lateral lobectomies. One re-resection is included. Liver resection was performed with hepatic pedicle clamping in 20 cases. Total vascular exclusion was never performed. Follow-up consisted of physical examination, CEA determinations, US and, in suspected cases, CT scan. Median follow-up was 26 months (range 3-102 months).

**Results:** there were no intraoperative deaths. One patient died in the postoperative period from hepatic failure. Postoperative complications included subphrenic abscess in 2 cases, biliary stricture in one case, transient ascites in 2 cases, urinary infection in 2 cases, pneumonia in one case. Median estimated operative blood loss was 600 mL. Overall 5-year survival rate was 24% (11 patients).

**Discussion and conclusions:** Patients affected by liver metastases from colorectal cancer who receive no treatment have a mean survival rate of 8.7 months. The only potentially curative treatment is resection. Predictors of survival are age and sex, CEA levels, stage of primary tumor, number of metastases, localization and size of metastases, extent of liver involvement, type of surgery, margins of resection, number of blood transfusion. Our experience confirms literature data of overall survival and low perioperative morbidity and mortality.

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